

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : A61K 31/715, A61M 1/28	A1	(11) International Publication Number: <b>WO 95/19778</b> (43) International Publication Date: 27 July 1995 (27.07.95)
(21) International Application Number: PCT/US95/01090 (22) International Filing Date: 23 January 1995 (23.01.95) (30) Priority Data: 08/184,813 21 January 1994 (21.01.94) US (71) Applicant: BAXTER INTERNATIONAL INC. [US/US]; One Baxter Parkway, Deerfield, IL 60015 (US). (72) Inventors: MARTIS, Leo; 5524 Old Wood Court, Long Grove, IL 60047 (US). BURKE, Ron; 2914 N. Mitchell, Arlington Heights, IL 60004 (US). SHOCKLEY, Ty; 1236 Cavell Avenue, Highland Park, IL 60035 (US). HENDERSON, Lee, W.; 725 N. Sheridan Road, Lake Forest, IL 60045 (US). FALLER, Bernardette; 11, route de Rouffach, F- 68000 Colmar (FR). (74) Agents: BORECKI, Thomas, S. et al; 1620 North Waukegan Road, McGaw Park, IL 60085 (US).	(81) Designated States: AU, BR, CA, CN, JP, KR, MX, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
(54) Title: PERITONEAL DIALYSIS SOLUTIONS CONTAINING MALTODEXTRINS AND AMINO ACIDS (57) Abstract  A peritoneal dialysis solution comprising as osmotic agents approximately 2.0 to about 6.0 % (w/v) maltodextrins and approximately 0.25 to about 2.0 % (w/v) amino acids. The peritoneal dialysis solution will also include other components such as sodium, chloride, lactate, bicarbonate, calcium, and magnesium.		

- 24 -

WE CLAIM:

1. A peritoneal dialysis solution comprising as osmotic agents:  
approximately 2.0 to about 6.0% (w/v) maltodextrins;  
5 and  
approximately 0.25 to about 2.0% (w/v) amino acids.
2. The peritoneal dialysis solution of Claim 1 wherein the amino acids comprise both essential and non-essential amino acids.
- 10 3. The peritoneal dialysis solution of Claim 1 including sodium, chloride, lactate, bicarbonate, calcium, and magnesium.
4. The peritoneal dialysis solution of Claim 1 wherein the solution includes:  
15 120 to about 140 (mEq/L) sodium;  
70 to about 110 (mEq/L) chloride;  
0 to about 45.00 (mEq/L) of lactate;  
0 to about 45.00 (mEq/L) of bicarbonate;  
0 to about 4.00 (mEq/L) of calcium; and  
20 0 to about 4.00 (mEq/L) of magnesium.
5. The peritoneal dialysis solution of Claim 1 wherein the pH of the solution is approximately 6.0 to 7.4.
6. The peritoneal dialysis solution of Claim 1  
25 wherein the maltodextrins have the following composition:  
Weight Average Mol. Wt. (Mw) 10,000 - 16,000 daltons  
Number Average Mol. Wt. (Mn) 4,000 - 8,000 daltons  
Polydispersity 1.0 - 4.0  

---

Fraction > 100,000 daltons NMT 1.0%  
30 Mono, Di, Trisaccharides NMT 5.0%  
Distribution normal  
Alpha (1-4) NLT 90%  
Aluminum (10% solution) <10ppb

- 25 -

Aqueous Solubility	NLT 10% (w/v)
pH (10% solution)	5.0 - 7.0
Heavy Metals	<5ppm
DP (Degree of polymerization)	
5 greater than 20	≥ 75%
DP greater than 50	≥ 50%
DP greater than 100	≥ 25%

7. The peritoneal dialysis solution of Claim 1 wherein the maltodextrins are derived from the hydrolysis of starch.

8. The peritoneal dialysis solution of Claim 1 wherein the amino acids comprise:

	<u>Amino Acid</u>	<u>Conc. (mg%)</u>
	Leucine	74 - 112
15	Valine	100 - 151
	Threonine	47 - 71
	Isoleucine	61 - 92
	Lysine.HCl	55 - 83
	Histidine	52 - 78
20	Methionine	32 - 48
	Phenylalanine	42 - 62
	Tryptophan	20 - 30
	Alanine	68 - 103
	Proline	43 - 65
25	Arginine	60 - 113
	Glycine	36 - 55
	Serine	48 - 72
	Tyrosine	20 - 35
	Aspartate	55 - 83
30	Glutamate	55 - 83

9. The peritoneal dialysis solution of Claim 1 wherein the amino acids are chosen so as to have the following ratios:

- 26 -

Phenylalanine/Tyrosine	1.3 - 3.0
------------------------	-----------

Essential/Total Amino Acids	0.4 - 0.7
-----------------------------	-----------

10. The peritoneal dialysis solution of Claim 1 wherein maltodextrins and amino acids comprise the only osmotic agents.

11. A peritoneal dialysis solution comprising:

Maltodextrins (% w/v)	2.0 - 6.0
Amino Acids (% w/v)	0.25 - 2.0
Sodium (mEq/L)	120 - 140
Chloride (mEq/L)	70 - 110
Lactate (mEq/L)	0.0 - 45.0
Bicarbonate (mEq/L)	0.0 - 45.0
Calcium (mEq/L)	0.0 - 4.0
Magnesium (mEq/L)	0.0 - 4.0
pH	6.0 - 7.4

12. The peritoneal dialysis solution of Claim 11 wherein the maltodextrins are derived from the hydrolysis of starch and have the following composition:

Weight Average Mol. Wt. (Mw)	10,000 - 16,000 daltons
Number Average Mol. Wt. (Mn)	4,000 - 8,000 daltons
Polydispersity	1.0 - 4.0
Fraction > 100,000 daltons	NMT 1.0%
Mono, Di, Trisaccharides	NMT 5.0%
Distribution	normal
Alpha (1-4)	NLT 90%
Aluminum (10% solution)	<10ppb
Aqueous Solubility	NLT 10% (w/v)
pH (10% solution)	5.0 - 7.0
Heavy Metals	<5ppm

---

DP (Degree of polymerization)	
greater than 20	≥ 75%
DP greater than 40	≥ 50%
DP greater than 80	≥ 25%

- 27 -

13. The peritoneal dialysis solution of Claim 11 wherein the amino acids comprise:

	<u>Amino Acid</u>	<u>Conc. (mg/l)</u>
	Leucine	74 - 112
5	Valine	100 - 151
	Threonine	47 - 71
	Isoleucine	61 - 92
	Lysine.HCl	55 - 83
	Histidine	52 - 78
10	Methionine	32 - 48
	Phenylalanine	42 - 62
	Tryptophan	20 - 30
	Alanine	68 - 103
	Proline	43 - 65
15	Arginine	60 - 113
	Glycine	36 - 55
	Serine	48 - 72
	Tyrosine	20 - 35
	Aspartate	55 - 83
20	Glutamate	55 - 83

14. The peritoneal dialysis solution of Claim 11 wherein the amino acids are chosen so as to have the following ratios:

	Phenylalanine/Tyrosine	1.3 - 3.0
25	Essential/Total Amino Acids	0.4 - 0.7

15. The peritoneal dialysis solution of Claim 11 wherein maltodextrins and amino acids comprise the only osmotic agents.

~~16. A method for providing an osmotic agent for a~~  
 30 peritoneal dialysis solution comprising the steps of selecting as the osmotic agent two compositions, one having a molecular weight equal to or greater than 10,000 daltons and comprising approximately 2.0 to about 6.0%

- 28 -

(w/v) of the composition and a second composition having a molecular weight equal to or less than 300 daltons and comprising approximately .25 to about 2.0% w/v of the composition.

5 17. The method of Claim 16 wherein the osmotic agent includes maltodextrin and amino acids.

18. The method of Claim 17 wherein the maltodextrins are derived from the hydrolysis of starch and have the following composition:

10	Weight Average Mol. Wt. (Mw)	10,000 - 16,000 daltons
	Number Average Mol. Wt. (Mn)	4,000 - 8,000 daltons
	Polydispersity	1.0 - 4.0
	Fraction > 100,000 daltons	NMT 1.0%
	Mono, Di, Trisaccharides	NMT 5.0%
15	Distribution	normal
	Alpha (1-4)	NLT 90%
	Aluminum (10% solution)	<10ppb
	Aqueous Solubility	NLT 10% (w/v)
	pH (10% solution)	5.0 - 7.0
20	Heavy Metals	<5ppm
	DP (Degree of polymerization)	
	greater than 20	≥ 75%
	DP greater than 50	≥ 50%
	DP greater than 100	≥ 25%

25 19. The method of Claim 17 wherein the amino acids comprise:

	<u>Amino Acid</u>	<u>Conc. (mg%)</u>
	Leucine	74 - 112
	Valine	100 - 151
30	Threonine	47 - 71
	Isoleucine	61 - 92
	Lysine.HCl	55 - 83
	Histidine	52 - 78

- 29 -

	Methionine	32 - 48
	Phenylalanine	42 - 62
	Tryptophan	20 - 30
	Alanine	68 - 103
5	Proline	43 - 65
	Arginine	60 - 113
	Glycine	36 - 55
	Serine	48 - 72
	Tyrosine	20 - 35
10	Aspartate	55 - 83
	Glutamate	55 - 83

20. A two part peritoneal dialysis solution designed to be mixed prior to infusion into a patient comprising:

15 a first part housed in a first structure including approximately 2.0 to about 6.0% (w/v) maltodextrin and a pH of approximately 4.0 to about 5.5;

a second part housed in a second structure including amino acids; and

20 including in either the first or the second structure a sufficient amount of the following ingredients so when the first part and second part are mixed the following is provided: 120 to about 140 (mEq/L) sodium; 70.0 to about 110.00 (mEq/L) chloride;  
25 0.0 to about 5.0 (mEq/L) lactate; 0.0 to about 45.0 (mEq/L) bicarbonate; 0.0 to about 4.0 mEq/L) calcium; and 0.0 to about 4.0 (mEq/L) magnesium.

21. The two part peritoneal dialysis solution of ~~claim 20 wherein the first and second structures are two~~  
30 separate chambers of a single container.

- 30 -

22. The two part peritoneal dialysis solution of Claim 20 wherein the pH of a resultant solution, comprising a mixture of the first part and the second part, is approximately 6.0 to about 7.4.

---